Establishment of Frontotemporal Dementia Patient-Specific Induced Pluripotent Stem (iPS) Cell Lines with Defined Genetic Mutations

Grant Award Details

Establishment of Frontotemporal Dementia Patient-Specific Induced Pluripotent Stem (iPS) Cell Lines with Defined Genetic Mutations

Grant Type: New Cell Lines

Grant Number: RL1-00650

Investigator:

Name:	Robert Farese
Institution:	Gladstone Institutes, J. David
Type:	PI

Disease Focus: Dementia, Neurological Disorders

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $1,696,424

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title:	Establishment of Frontotemporal Dementia Patient-Specific Induced Pluripotent Stem (iPS) Cell Lines with Defined Genetic Mutations
Public Abstract:	We propose to generate induced pluripotent stem (iPS) cells from skin cells derived from human subjects with frontotemporal dementia (FTD). FTD accounts for 15–20% of all dementia cases and, with newly identified genetic causes, is now recognized as the most common dementia in patients under 65 years of age. FTD patients suffer progressive neurodegeneration in the frontal and temporal lobes and other brain regions, resulting in behavioral changes and memory and motor neuron deficits. The median age of onset for this devastating disease is 58 years, and disease progression is rapid, with death in 3–8 years. Compared with other age-dependent neurodegenerative diseases, the molecular, cellular, and genetic bases of FTD remain poorly understood. Genetic causes are estimated to account for ~40% of FTD. In addition to tau identified in 1998, mutations in three causative genes have been identified during the last three years. The identification of FTD mutations opens exciting new avenues for understanding the causes of FTD. Research on these mutations will help to identify effective therapies. However, the ability to study the functions of these factors is severely limited due to the lack of available human neurons from FTD patients. To address the need for disease– and patient–specific neurons, we will use the powerful new technique of iPS cells. iPS cells are derived from skin cells and can be used to generate any cell types in the body, including neurons. We will obtain human skin cells from FTD patients with disease-causing mutations and generate many FTD mutation–specific iPS cell lines. We will then use these iPS cells to generate FTD mutation–specific neurons to study disease mechanisms. The bank of iPS cell lines we generate will also enable the development of sensitive assays for drug screening and testing of therapeutic agents for treating FTD. All cell lines will be made available to the global FTD research community. The generation of human neurons from FTD patients will be a tremendous advance toward finding a cure for this disease.
Statement of Benefit to California:	California is the U.S. leader in basic research into stem cell–based therapies for disease. To help California remain at the forefront of research on neurological disease, we propose to use induced pluripotent stem (iPS) cells—a revolutionary new technique developed recently by Dr. Shinya Yamanaka—to target frontotemporal dementia (FTD). FTD is a devastating and common form of dementia. {REDACTED} The proposed research will establish California as the leader in generating human patient–specific neurons from iPS cells. The potential long-term benefits to California include growth of the clinical enterprise in the diagnosis and treatment of FTD, the establishment of biotechnology to generate new drugs for FTD, and potential intellectual properties for driving private enterprises to develop therapies.